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Synthesis of Pseudoaromatic Expanded Porphyrin Analogues

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Optically active expanded porphyrins bearing thiophene were synthesized by Schiff base forming reaction. The condensation of thiophene containing 1,14-bisformyl tripyrrane with aromatic diamines failed to give desired macrocycles but condensation with aliphatic 1,2-diamines gave the desired products. The macrocycles synthesized tend to maintain 18π system and the ethylene bridge shows somewhat resistance toward oxidation.

Expanded porphyrins and their metal complexes are new type of macrocycles with many potential uses.[1] The successful synthesis of the pentaaza-expanded porphyrins and their metal complexes in 1987[2] provided a new class of materials with physical properties different from the meso-porphyrins. For example, the lanthanide complexes in aqueous solution have been used as magnetic resonance imaging (MRI)[3] and selective anion binding.[4] Chiral recognition of amino acids by chiral porphyrins has been reported[4d] and multiple recognition hosts can be constructed using expanded porphyrins with intrinsic chirality. The expanded porphyrins are considered to be aromatic 22π benzannulene systems. The controlled modification of the basic framework of these porphyrins while maintaining their aromatic character should allow for the systematic variation of the spectroscopic properties and the energy of the molecuar orbitals. The construction of new optical materials requires precise control of orbital energeties and the electronic states of the molecules. One method of controlling the orbital energy of porphyrin macrocycles is to replace the core nitrogens with other heteroatoms. Insertion of other heteroatoms for the core nitrogens in the porphyrins changes the molecular symmetry and the electronic transition energy. We are interested in the development of synthetic methods for the preparation of core-modified porphyrins.[5-7] A key step in our synthesis involved the condensation of 16-oxatetrahydrotripyrrin or 16-thiatetrahydrotripyrrin derivatives with 2,5-bis(α-hydroxymethyl)pyrrole to give the corresponding core-modified porphyrins. The desired tripyrranes were obtained by the acid catalyzed condensation of 2,5-bis[(α-hydroxy-α-mesityl)methyl]thiophene with excess pyrrole. Because we were able to synthesize tripyrranes in two steps with high yields we have investigated related methods for synthesizing various core-modified expanded porphyrins with predesignated orientation of the core ligands. In this paper, we report a convenient synthesis of core-modified expanded porphyrins bearing one thiophene moiety. The introduction of sufur produced a new class of macrocycles exhibiting pseudo-macroaromatic character and chirality.

The bis-hydroxymethylation of thiophene via lithiation is well-established reaction.[8] 5,10-Diphenyl-16-thia-5,10,15,17-tetrahydrotripyrrin (**4**) and 5,10-dimesityl-16-thia-5,10,15,17-tetrahydrotripyrrin (**5**) were easily synthesized by condensing the corresponding bis-diol (**2**) and (**3**) with excess pyrrole in the presence of BF_3:$O(Et)_2$.[7,9] Vilsmeier formylation of either (**4**) or (**5**) gave the key intermediates (**6**) and (**7**) in 62% and 66%, respectively (Scheme 1). The final step in the synthesis is the acid catalyzed imine formation of the appropriate 1,2-diamines (**8**), (**9**) with either (**6**) or (**7**) to afford the macrocycle (**10**), (**11**) and (**12**) (Scheme 2). The formation of the desired Schiff bases was not straightforward and some exploratory work were required to find the appropriate conditions. The use of various protic acids and solvents failed to give desired product and even metal salt, $CdCl_2$[2b] as

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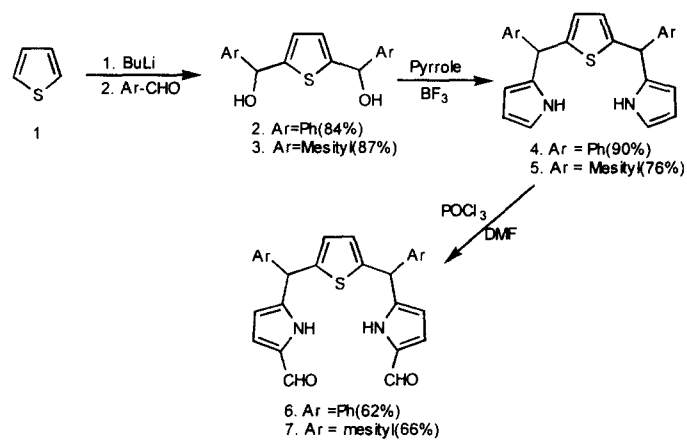
a potential template gave only unreacted starting material. We found that the reaction proceeded readily in the presence of an excess of powdered molecular sieves. As the condensation proceeded, the reaction mixture colored a bright red-purple. The molecular sieves may act as a catalyst, dehydrating agent, templating agent, or any combination of these effects. During the condensation with powdered molecular sieves the meso-positions of the macrocycle were oxidize. But complete oxidation did not occur because the resulting fully oxidized macrocycle would be anti-aromatic.

Scheme 1

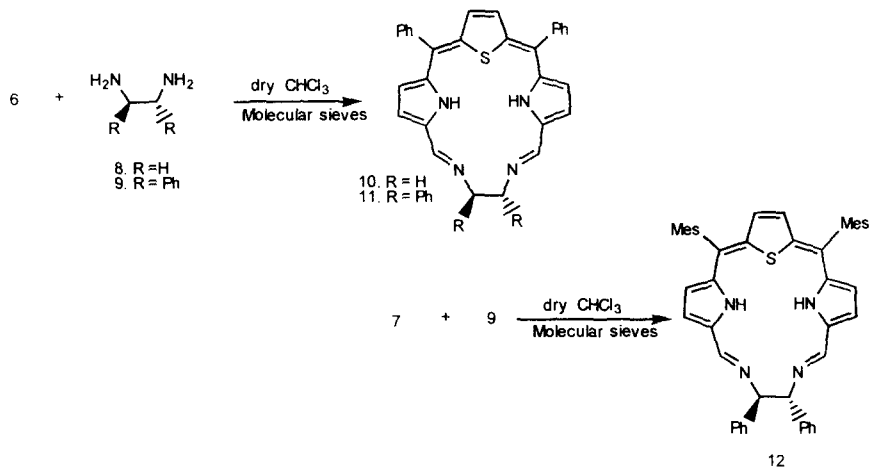


The condensation was not successful when aromatic 1,2-diamine such as phenylene diamine was employed.

The UV-vis spectrum shows Soret-like band at 380 nm and Q-bands (Figure 1). The electronic spectra are somewhat different from that of meso-5,10,15,20-tetraphenylporphyrin (TPP) but the pattern of spectrum seems to indicate weak aromatic character of the macrocycles. The ethylene bridge was somewhat resistant toward oxidation. Attempted oxidation with DDQ, p-chloranil or protons sponge[3b] was not successful. Only extensive decomposition of macrocycles was observed in all attempts. This is possibly due to the pseudoaromatic character of (**12**). Compound (**12**) seems more stable under acidic conditions than (**11**). Macrocycle (**11**) was hydrolysed back to starting materials during column chromatographic separation while (**12**) was intact. The bulky *meso*-substituents in (**12**) possibly prevent the double bond migration and make the structure more rigid and resistant toward hydrolysis. The proton NMR spectrum of (**12**) did not show any visible sign of macrocyclic ring current. The pyrrolic N-H signals were not observed at room temperature and two β-pyrrolic hydrogens appeared as broad singlets. Obviously, the molecule is quite flexible and fluctuating. The shapes of resonance lines are closely related with the exchange rates and fluctuational motion of the compounds. The two-fold symmetry of the molecule at room temperature was dramatically changed at the probe temperature of 223K. The proton NMR spectra taken at 223K indicated that the compound lose its symmmetry. All equivalent signals at room temperature were clearly separated and were not equivalent anymore. For example, the two pyrrolic N-H signals appeared at 9.59 and 8.08 ppm which were completely disappeared after addition of D_2O. Two benzylic protons also break down to doublets of doublet. The aromatic character of the compound was confirmed by independent synthesis of furan containing compound (**13**) that is corrin-type aromatic system.[10] UV-Vis spectrum of (**13**) is almost identical with (**12**) as shown in Figure 1. The Soret-like band of (**13**) (λ_{max} = 381 nm) matches well with (**12**) (λ_{max} = 380 nm) each other. More systematic studies will be necessary for the complete verification of the aromaticity of (**12**).

The obvious advantages of the present syntheses are their wide applicabilities in synthesizing chiral expanded porphyrinoids having hetero ligands in the core and meso-substituents in the periphery. The synthetic approaches presented with this article also could be applied to the synthesis of macrocycles bearing regiospecifically substituted pyrrole units.[11] Our demonstration for the synthesis of core-modified, meso-substituted expanded porphyrins in simple manner will be applicable in designing unique macrocyclic systems with intrinsic chirality.

Scheme 2



Currently, we are investigating the possibility of synthesizing other core-modified porphyrins and expanded porphyrins associated with various aromatic heterocycles using the same synthetic analogy described here. The chemistry and electronic properties of their metal complexes are under investigation.

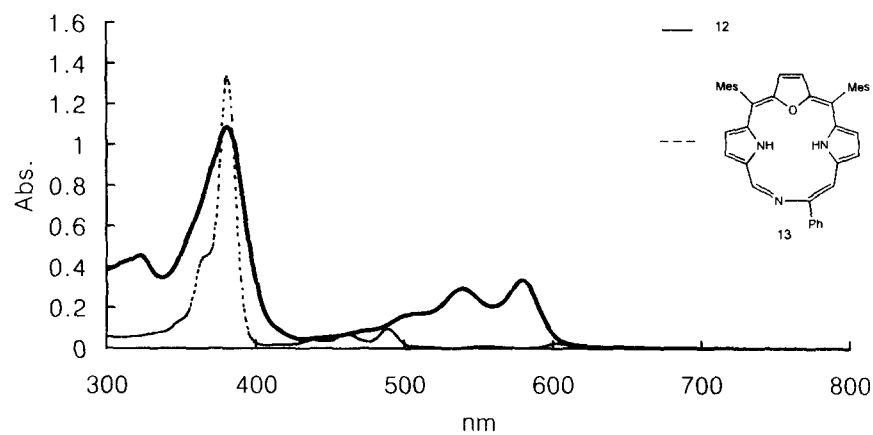


Figure 1. UV-Vis Spectra of macrocycle **12** (2.80 x 10^{-4} M) and **13** (2.90 x 10^{-6} M) in methylene chloride.

Acknowledgement

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10. Abstract of the synthesis and characterization of this compounds has been submitted to the KCS fall meeting Oct. 23 (1998).

11. **10**: 1,14-Bisformyl-5,10-diphenyl-16-thiatripyrromethane (50 mg, 0.11 mmol) and ethylene diamine (8 ml, 0.11 mmol) was dissolved in chloroform (50 ml). Then molecular sieve (type 4A, powder, 5.0 g) was added and the heterogeneuos mixture was stirred at 60 °C for 24 hr. The molecular sieve was removed by filteration and the solvent was evaporated in vaccuo. The resulting dark red solid was purified by column chromatography on silica (ethyl acetate/triethylamine=19/1). Yield 15 mg (20%); ^{1}H NMR ($CDCl_3$) δ 8.19 (s, 2H, thiophene-H), 7.50-7.26 (m, 10H, phenyl-H), 6.91 and 6.31 (two doublets, 4H, pyrrolic-H), 6.86 (s, 2H, imine), 4.02 (s, 4H, ethylene-H); .FAB MS Calculated for $C_{30}H_{24}N_4S$ 472.60, Found; 472.00. **11:** A sample of 1,14-bisformyl-5,10-diphenyl-16-thiatripyrromethane (50 mg, 0.11 mmol) and (1R,2R)-(+)-1,2-diphenylethylene diamine (23 mg, 0.11 mmol) was treated identically as for (**10**). Column chromatography on silica (methylene chloride) affords 28 mg (40 %) of pure product. ^{1}H NMR ($CDCl_3$) δ 7.85 (s, 2H, thiophene-H), 7.52-7.24 (m, 20H, phenyl-H), 6.91 (s, 2H, imine), 6.79 and 6.31 (two doublets, 4H, pyrrolic-H), 5.22 (s, 2H, methine),. FAB MS Calculated for $C_{42}H_{32}N_4S$ 624.08, Found; 624.00. **12**: A sample of 1,14-Bisformyl-5,10-dimesityl-16-thiatripyrromethane (50 mg, 0.09 mmol) and (1R,2R)-(+)-1,2-diphenylethylene diamine (19 mg, 0.09 mmol) was treated identically as for (**10**). This compound was acid stable. Column chromatography on silica (methylene chloride) affords 32 mg (50 %) of pure product. ^{1}H NMR ($CDCl_3$) δ 7.79 (s, 2H, thiophene-H), 7.33-7.20 (m, 10H, phenyl-H), 6.95 (s, 4H, Ar(mesityl)-H), 6.76 and 6.09 (two doublets, 4H, pyrrolic-H), 6.53 (s, 2H, imine), 5.14 (s, 2H, methine), 2.35 and 2.09 (s, 18H, methyl). UV-vis λ_{max} ($\varepsilon \times 10^{-4}$) 322(1.63), 381(3.88), 503(0.117), 538(1.05), 579(1.20). FAB MS Calculated for $C_{48}H_{44}N_4S$ 708.96, Found; 709.22.